

Signal-dependent incorporation of MyoD-BAF60c into Brg1-based SWI/SNF chromatin-remodelling complex.

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Public Summary:

Tissue-specific transcriptional activators initiate differentiation towards specialized cell types by inducing chromatin modifications permissive for transcription at target loci, through the recruitment of SWI/SNF chromatin-remodelling complex. However, the molecular mechanism that regulates SWI/SNF nuclear distribution in response to differentiation signals is unknown. We show that the muscle determination factor MyoD and the SWI/SNF subunit BAF60c interact on the regulatory elements of MyoD-target genes in myoblasts, prior to activation of transcription. BAF60c facilitates MyoD binding to target genes and marks the chromatin for signal-dependent recruitment of the SWI/SNF core to muscle genes. BAF60c phosphorylation on a conserved threonine by differentiation-activated p38 α kinase is the signal that promotes incorporation of MyoD-BAF60c into a Brg1-based SWI/SNF complex, which remodels the chromatin and activates transcription of MyoD-target genes. Our data support an unprecedented two-step model by which pre-assembled BAF60c-MyoD complex directs recruitment of SWI/SNF to muscle loci in response to differentiation cues.

Scientific Abstract:

Tissue-specific transcriptional activators initiate differentiation towards specialized cell types by inducing chromatin modifications permissive for transcription at target loci, through the recruitment of SWI/SNF chromatin-remodelling complex. However, the molecular mechanism that regulates SWI/SNF nuclear distribution in response to differentiation signals is unknown. We show that the muscle determination factor MyoD and the SWI/SNF subunit BAF60c interact on the regulatory elements of MyoD-target genes in myoblasts, prior to activation of transcription. BAF60c facilitates MyoD binding to target genes and marks the chromatin for signal-dependent recruitment of the SWI/SNF core to muscle genes. BAF60c phosphorylation on a conserved threonine by differentiation-activated p38 α kinase is the signal that promotes incorporation of MyoD-BAF60c into a Brg1-based SWI/SNF complex, which remodels the chromatin and activates transcription of MyoD-target genes. Our data support an unprecedented two-step model by which pre-assembled BAF60c-MyoD complex directs recruitment of SWI/SNF to muscle loci in response to differentiation cues.

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